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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,613	01/30/2006	Richard G Vile	07039-444US1	6311

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FISH & RICHARDSON P.C.
PO BOX 1022
MINNEAPOLIS, MN 55440-1022

EXAMINER	
HIRIYANNA, KELAGINAMANE T	
ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
02/21/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,613	VILE ET AL.	
	Examiner	Art Unit	
	KELAGINAMANE T. HIRIYANNA	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,5,39 and 40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,5,39 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/26/2007 has been entered.

Applicant's response filed on 11/26/2007 in response to office action mailed on 11/15/2007 has been acknowledged.

Claims 2, 5, and 39-40 *are pending and are examined in this office action. Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is* ***571-273-8300.***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 103

Claims 2, 5 and 39-40 are rejected under 35 USC 103 (a) as being unpatentable over Curiel et al (2000, Clinical Cancer. Res. 6:3395-3399; art of record) in view of (*WO 98/5936*; art of record) and Dean et al (2001, Molecular and Cellular Biology 21:721-730).

The above claims are directed to a viral vector comprising a nucleic acid encoding a therapeutic polypeptide that is an essential gene product that allows virus to replicate wherein said nucleic acid is operably linked to a TNF-alpha 3'UTR destabilizing element that enhances the expression of said polypeptide in target cells relative to a

non-target cell and in further limitations the target cell is a tumor cell and the viral vector is a adenoviral vector or a vaccinia virus vector.

Curiel teaches regarding the development of a conditionally replicative Adenovirus for cancer therapy (p.3395, abstract) wherein a tumor cell killing by the viral agent is achieved by a direct consequence of the viral replication and the relative sparing of non-tumor cells. To this end Curiel teaches using conditional replication of Adenovirus (CRAD) by engineering the specificity of replication based on transcriptional control (p.3396, col.1-2 bridging p.3397)). Regarding implementation of the same Curiel further teaches engineering a adenoviral vector with the specificity conditionality of replication based on transcriptional control of E1A gene for treating cancer cells (Abstract; Fig.1, Table 1; p.3396-97). Curiel however does not teach the use of mRNA destabilizing elements in engineering of E1A polypeptide expression for a conditional replication of the virus used for tumor therapy.

Regarding claims limitation of using mRNA destabilizing elements for conditional expression of therapeutic genes *WO 98/5936* teaches compositions of recombinant viral vectors including adenoviral and retroviral vectors for gene therapy of tumors etc., (abstract, p.1, and p.18, 2nd paragraph) comprising therapeutic polypeptide coding sequences (p.11, 2nd paragraph bridging p.12, 1-2ndparagrph) with heterologous regulatory sequences derived from 3' untranslated region of vascular endothelial growth factor (VEGF) gene (abstract, p.1 and entire document) and wherein which said regulatory sequences are involved in hypoxia- regulated modulation (expression) of the therapeutic gene in target cells (p.5, 2nd paragraph). *WO 98/5936* further teaches hypoxia-mediated expression of the cloned genes with said regulatory elements in tumors of syngenic Fischer 344 rats (p.34, 2nd paragraph). However, *WO 98/5936* does not teach TNF-alpha 3' UTR sequences as destabilizing elements, its stabilization in proliferating cells or its reposiveness to RAS and P-MAPK activity and conditionally replicative Adenovirus.

Dean teaches regarding 3'UTR mRNA destabilizing sequences present in TNF-alpha (p.721, col.1, 2nd and 3rd paragraphs bridging col.2; abstract) and their

involvement in the regulation of mRNA stability and expression (Abstract; p. 726-727, col.1; entire article).

Thus it would have been obvious for one of ordinary skill in the art to incorporate into the conditionally replicative Adenoviral vector E1A gene constructs of Curiel a 3'UTR conditional mRNA stabilizing elements as taught by *WO 98/5936* wherein 3'-UTR sequences are derived from TNF-alpha gene as taught by Dean and treat tumors. One skilled in the art would have been motivated to do so as the 3'UTR elements selectively stabilize and enhance the therapeutic genes in engineered viral vectors used in suicidal cancer therapy. One of ordinary skill in the art would have reasonable expectation of success of making and using the viral vectors incorporating said 3'UTR elements for treating tumor because of the art teaches that it is routine use conditional replicative virus of cancer therapy and further art teaches the therapeutic genes can be differentially expressed in target cells (tumor cells) and non-target cells (normal cells) using certain 3' UTR sequences including that of TNF-alpha mRNA. Thus, the claimed invention was *prima facie* obvious.

Conclusion:

No claim allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Kelaginamane Hiriyanna* whose telephone number is **(571) 272-3307**. The examiner can normally be reached Monday through Friday from 9 AM-5PM. Any inquiry concerning this communication or earlier communications regarding the formalities should be directed to Patent Analyst *William N. Phillips* whose telephone number is ***571 272-0548.*** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Joseph Woitach*, may be reached at **(571) 272-0739.** The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). When calling please have your application serial number or patent number, the type of document you are having an image problem with, the number of pages and the specific

nature of the problem. For all other customer support, please call the USPTO call center (UCC) at (800) 786-9199.

Kelaginamane T. Hiriyanna
Patent Examiner
Art Unit 1633

Joe Woitach
AU1633